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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,044	09/17/2003	Katsuya Satoh	001458.00037	2743

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EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/664,044	SATOH ET AL.	
	Examiner	Art Unit	
	David A. Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6 and 9-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6 and 9-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Amendment of 9/17/03 has been entered. Claims 1-2, 5-6 and 9-16 are pending. Claims 1-2, 5-6 and 9-16 are under examination. The amendment has entered no new matter.

Claims 1 and 5 are objected to under 37 CFR 1.75(i), as being of improper form for failing to indent each step or element of the claims.

Claims 12 and 16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 12 and 16 recite precisely the same limitations as base claims 10 and 14, respectively.

Claims 1-2, 5-6 and 9-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant was not in possession of the genus of PrpA proteins, nor of any of the active fragment(s) thereof, that would bind to a DNA strand break.

Claims 1, 5 and 9-16 encompass the use or provision of any protein with DNA strand break binding activity that can be derived from Deinococcus radiodurans. Applicant has disclosed no protein, except for that having the instantly disclosed amino acid sequence of SEQ ID NO: 1, as having this binding activity. If any other such binding proteins might exist, one would not be able to a priori know how they would be structurally related to the PrpA protein having SEQ ID NO:1. The instantly disclosed PrpA protein having SEQ ID NO:1 is thus not representative of the genus of PrpA proteins with DNA strand break binding activity that might be derived from Deinococcus radiodurans.

Further, with respect to the PrpA protein of SEQ ID NO:1, applicant has disclosed no variants thereof that have DNA strand break binding activity. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, the instant disclosure is limited to the protein having the amino acid sequence of SEQ ID NO: 1. A protein having this particular sequence, as recited in instant claims 2 and 6, is thus the only PrpA protein derived from Deinococcus radiodurans that has been adequately described.

Furthermore, all of claims 1-2, 5-6 and 9-16 encompass the use of a fragment of the PrpA protein with DNA strand break binding activity that can be derived from Deinococcus radiodurans. Even for the case in which the protein is limited to a protein of SEQ ID NO:1 applicant's disclosure has not described any fragments thereof that have the required binding activity. Applicant has not related any structural features of the protein of SEQ ID NO:1 to its capacity for binding DNA strand breaks. Therefore one would not be able to envision the structural features of any of the binding fragments contemplated by applicant. While it might be routine for one of skill to screen for such binding fragments, the ability to identify a composition by screening methods does not describe the composition that would be identified. See Univ. of Rochester 69 USPQ2d 1886. Applicant has thus not described the fragments of PrpA that would be used as DNA strand break binding agents in the claimed method or provided as such agents in the claimed kit.

Claims 1, 5, and 9-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the case in which the PrpA protein is one having SEQ ID NO: 1, does not reasonably provide enablement for the case in which the PrpA protein is one having an amino acid sequence other than that of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to practice the method or make the kit of the invention commensurate in scope with these claims.

Claims 1, 5 and 9-16 encompass use of any PrpA protein with DNA strand break binding activity that can be derived from Deinococcus radiodurans (In stating this rejection, the examiner considers recitation of "derived from" to broadly refer to any protein having DNA strand break binding activity that can be isolated, in its natural state, from Deinococcus radiodurans. Additionally, the examiner considers "derived from" to broadly encompass any derivatized forms of such isolated proteins; thus any such isolated protein could be modified by chemical derivatizing techniques or by genetic engineering). Applicant has disclosed no PrpA protein, except for that having the instantly disclosed amino acid sequence of SEQ ID NO:1, as having this binding activity. Furthermore, with respect to this particular PrpA protein, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the various derivatives thereof that might be obtained thereof. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, instantly the disclosure is limited to the PrpA protein having the amino acid sequence of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein, and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. The specification does not support the broad scope of the claims which encompass all derivatives of instant SEQ ID NO: 1. because applicant has not identified (A) the residues/regions of instant SEQ ID

NO:1 critical for DNA strand break binding activity; (B) the general tolerance of DNA strand break binding proteins to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of DNA strand break binding protein with an expectation of obtaining the desired binding function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the DNA strand break binding activity required by the claims and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, in Merz et al (eds.), Birkhauser, Boston, MA, pp. 433 and 492-495, cited on Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those proteins having DNA strand break binding activity required to practice the claimed method.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the use of any DNA strand break binding protein. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those derivatives having the desired biological characteristics is unpredictable, and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400.

Claims 1-2 and 5-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant was not in possession of the genus of "means for detecting the PrpA protein or a fragment thereof."

Applicant's disclosure has merely taught the provision of antibodies, either monoclonal or polyclonal, as such "means for detecting". Antibodies, as a subgenus of proteins, are not representative of the full genus of high and low molecular weight compounds that might be capable of detecting the PrpA protein. Applicant has disclosed nothing about the structural features of the PrpA protein of SEQ ID NO:1 that indicates that this sequence has any known motifs that might interact/bind with other known proteins. Applicant has disclosed nothing about this sequence that indicates that this sequence has any known motifs that might interact/bind with known low molecular weight compounds, such as cofactors/prosthetic groups.

While one of skill might be able to screen libraries of natural or synthehtic compounds that would bind to the PrpA protein, the ability to identify such a compound by screening methods does not describe the compound that would be identified. See Univ. of Rochester... 69 USPQ2d 1886.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 5-6 and 13-16 are rejected under 35 U.S.C. 102(a) or (e) as being anticipated by Narumi et al (JP 2003052376 or US 2003/0143707 A1).

The JP and the US documents are equivalent in disclosure (see Derwent abstract cited on Form 892). Only the US document is supplied with this action. The JP document is cited under 102 (a). Applicant cannot rely upon the foreign priority papers to overcome the rejection under 102 (a) because a translation of said papers has not been made of

record in accordance with 37 CFR 1.55. See MPEP § 201.15. The US document is cited under 102(e), since the inventive entity is different from that instantly.

Narumi et al disclose a kit containing the PrpA protein and an antibody thereto; see para. [0055]. The PrpA protein of the reference has the same sequence as that instantly. The antibody may be monoclonal or polyclonal; see para. [0049]. All components of the instant kits are thus shown.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Namuri et al in view of Chaubron et al (US 6,309,838).

Namuri et al have been noted supra for teaching the PrpA protein and antibodies of the instant kits. They teach that these reagents may be used to detect strand breaks in DNA; see, for example, para. [0055]. They do not give the details of the steps involved. Chaubron et al show the steps that one can use in the case in which one uses a DNA binding protein (ligand) that recognizes DNA damage, including strand breaks, and also uses an antibody to detect the protein (ligand) bound to damaged DNA. See, for example, col. 2, line 60-col. 3, line11; col. 9, lines 25-36; col. 10, lines 1-19 and 50-62. Since the PrpA protein of Namuri et al is one that binds to damaged DNA, and is thus a member of the genus of DNA binding proteins (ligands) taught by Chaubron et al, it would have been obvious to use the PrpA protein of Namuri et al in any detection method taught by Chaubron et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-

272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 6/22/06 DAS

David A Saunders

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